A RADIOBIOLOGICAL STUDY OF SOME INSECTICIDAL DERIVATIVES OF DIETHYL PHOSPHORIC ACID

BY

CLIFFORD CREIGHTON ROAN

B.S., University of Illinois, 1947
M.S., University of Illinois, 1947

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN ENTOMOLOGY
IN THE GRADUATE COLLEGE OF THE
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Introduction

The insecticidal organic phosphates and their analogues and homologues are exceptionally well suited for the application of radioactive tracer techniques to toxicological studies of their effects on selected test organisms. The ready availability of the radioactive isotope of phosphorus, P32, and the relative ease with which this isotope may be incorporated in the molecules of such compounds as tetraethyl pyrophosphate (TEP) and O,O-diethyl-O,*p*-nitrophenyl phosphate (Para-Oxon) makes radiobiological studies a valuable tool in investigating their mode of action.

We have been successful in preparing four such organic phosphates tagged with P32, i.e. TEP, Para-Oxon, tetraisopropyl pyrophosphate (TiP), and tetra-*n*-butyl pyrophosphate (TBP). These compounds have been employed in an investigation of their permeabilities, transport and metabolism in the American roach, *Periplaneta americana.*

Experimental Procedures

The compounds used in this study were synthesized from radioactive elemental red phosphorus employing the following basic reactions.

$$\text{I.}\quad P_4 + 6Cl_2 \xrightarrow{PCl_3} 4PCl_3$$

$$\text{II.}\quad 3ROH + PCl_3 \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}H + RCl + 2HCl$$

$$\text{III.}\quad (RO)_2\overset{\overset{O}{\|}}{P}H + Cl_2 \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}Cl + HCl$$

IV. $2(RO)_2\overset{\overset{O}{\|}}{P}Cl$ + pyridine $\longrightarrow$ $(RO)_2\overset{\overset{O}{\|}}{P}O\overset{\overset{O}{\|}}{P}(OR)_2$ + pyridine hydrochloride

V. $(RO)_2\overset{\overset{O}{\|}}{P}Cl$ + sodium *p* nitrophenoxide $\longrightarrow$ O,O-dialkyl-O,*p*-nitrophenyl phosphate + NaCl

R = CH_3CH_2OH; $\begin{matrix}CH_3\\CH_3\end{matrix}>CHOH$; $CH_3CH_2CH_2CH_2OH$

Reaction IV was employed to synthesize TEP, TiP, and TBP. Reaction V was employed to synthesize Para-Oxon. Reaction I is based on the work of Forbes, et al (1946). Reactions II, III, V are based on a personal communication from Toy (1949). Reaction IV is based on Toy (1948).

Adult American roaches, *Periplaneta americana,* of uniform age were employed for these tests. Unless otherwise specified the males of the species were used. The roaches were treated topically on the ventral cervical membrane with various solutions of the compounds by the method of Trevan (1922).

Treated roaches were sacrificed at selected time intervals by freezing in "dry ice". Entire roaches or fractions thereof were wet-ashed in concentrated nitric acid and diluted to a constant volume. One milliliter aliquots were placed in aluminum capsules and evaporated to dryness for assaying with a Geiger-Mueller counter. The procedures followed were those recommended by Kamen (1947).

Summary

These compounds were employed in studies of their permeability, transport and metabolism. The effects of four solvents, propylene glycol, ethyl alcohol, dioxane and benzene on the rates of penetration of these compounds were investigated. Benzene gave consistently slower penetration rates following

topical applications to the ventral cervical membrane.

The rate of distribution throughout the body closely parallels the water solubilities of these materials, i.e. TEP>TiP>TBP>Para-Oxon. There was a pronounced tendency for concentration of the compounds in the region of the abdomen at one hour after treatment. Qualitative tests indicated the presence of the radioactive materials in the blood of the roach.

All four compounds were rapidly voided from the body of the test insect following a topical application. Solubility studies indicated that the excreted materials were inorganic in nature. The rates of excretion closely parallels the susceptibility of these compounds to aqueous hydrolysis, i.e. TEP>TBP>TiP>Para-Oxon.

BIBLIOGRAPHY

Forbes, M. C., C. A. Roswell, and R. N. Maxson (1946). Preparation of phosphorus trichloride (PCl_3). Inorganic Syntheses 2:145-147.

Kamen, M. C. (1947). Radioactive tracers in biology. Academic Press, N. Y., xiii & 281 pp.

Toy, A. D. F. (1948). The preparation of tetraethyl pyrophosphate and other tetraalkyl pyrophosphates. J. Amer. Chem. Soc., 70:3882.

Toy, A. D. F. (1949). Personal communication.

Trevan, J. W. (1922). An apparatus for the measurement of small quantities of fluid. Lancet. (London) 202:786.

VITA

Clifford C. Roan was born December 22, 1920 in Casey, Illinois. He completed his primary education in the rural schools of Clark County and was graduated from Casey Township High School in 1939. In September, 1939 he enrolled in the University of Illinois. In January, 1942 he enlisted in the United States Air Force, where he served until November, 1945.

In February, 1946 he reentered the University of Illinois. In February, 1947 he received a Bachelor of Sciences degree from the Division of Special Services for War Veterans of the University of Illinois. In October, 1947 he received a Master of Sciences degree in Entomology.

During the period of his graduate studies he worked as a research assistant for Dr. C. W. Kearns of the Entomology Department.

He was married to Chlorene Shick in Casey, Illinois, December 27, 1945. Their son Richard Lee was born April 1, 1947 in Chicago, Illinois.

He is a member of Phi Sigma Biological Society, an Associate member of Sigma Xi, a member of the American Association of Economic Entomologists, and a member of the American Chemical Society.

Publications: Roan, C. C. and C. W. Kearns, 1948. Testing insecticidal sprays. Soap and Sanit. Chem., 22:133-150.

Roan, C. C., H. E. Fernando, and C. W. Kearns, 1949. A radiobiological study of four organic phosphates. Submitted to J. Econ. Entomology.